THE ALKALI SALTS OF TRIBROMGUAIACOL.

A THESIS SUBMITTED TO THE FACULTY OF THE GRADUATE SCHOOL OF THE UNIVERSITY OF MINNESOTA BY GRACE M. BELL, IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE.

May 25, 1911.

Some time ago in working with a solution of tribromguaiacol in anhydrous acetone[1] it was found that the addition of solid potassium hydroxide produced a crystalline salt. The presence of the slightest amount of water caused the formation of a white salt. Preliminary analyses gave numbers corresponding to a potassium salt plus a molecule of water, while the color of the solid was decidedly different from that of the colorless water solution made by dissolving tribromguaiacol in dilute potassium hydroxide. This suggested the possibility of the existence of two isomeric salts, a white and a yellow.

The formation of potassium salts was studied in the following solvents: acetone, ether, water, alcohol, methyl alcohol and benzene.

The study of the action in acetone showed that an acetone solution of tribromguaiacol gave both yellow and white salts with solid potassium hydroxide. Neither could be obtained pure under any conditions found for obtaining

.....

[1] Torrey & Hunter, J. Am.Chem. Soc. 33, 194(1911)

it, and yellow salt always turned white on drying after removal from acetone

With ethyl ether and methyl alcohol, results were practically the same.

Work with a water solution of potassium hydroxide, adding tribromguaiacol directly to it, showed that with heat the yellow salt formed in all concentrations. With contentration of 7.5 o/o KOH, the salt formed, dissolved, while above this, it was relatively insoluble. All these alkaline solutions were yellow when hot but lost color when cold.

The salt was next made from alcoholic potash and an alcoholic solution of the phenol. Results were no better; the presence of both salts was indicated at the time of formation of the crystals and after drying. Both salts were found to be comparatively inactive with alkaline reagents.

Results from benzene showed a more stable product. A solution of potassium ethylate added to tribromguaiacol in benzene yielded practically pure yellow substance which

was analyzed for potassium and bromine, giving indications of an anhydrous form. In addition the salt was found to be inactive with ordinary reagents and unaffected by high temperature.

The sodium and the ammonium salts of the phenol were then made, both were white. Analyses proved them anhydrous. The ammonium salt melted sharply, while the sodium salt was more stable, acting somewhat like the potassium salt. That is, it turned yellow on heating but unlike the potassium salt the entire mass changed back to white on cooling.

The potassium salts of other phenols were prepared, all were white except tetrabromguaiacol the salt of which was yellow.

The most significant feature of these salts is the heat change, and the fact that both may exist together under a variety of conditions; that is, in an acetone solution, in moisture and carbon dioxide free air, under reduced pressure, and in the air of the laboratory. The conditions governing the formation of the yellow salt can be controlled; that is, by means of heating or with

metallic potassium in alcohol, but there is no definite way to obtain a homogeneous white salt. So it would seem that the yellow and the as yet unanalyzed white salt, are isomeric. Considering what kind of isomers they are, it would be well to give some of the more recent classifications and definitions of isomerism, to see if this is a correct explanation of their occurrence.

Kruyt[1] says two substances may be said to be isomeric when they have the same composition but show different properties under the same independently variable conditions. Accordingly, he finds there are, broadly speaking, three groups or kinds of isomerism, thus recognizing physical and chemical isomerism, the old categories, but differentiating chemical isomerism to two kinds: one, involving two distinct components and the other a shifting of the radical within the molecule. He has classified isomerism as follows:

I. Phase Isomerism.- corresponding largely to physical isomerism

.....

[1] B. 3, 540 (1910)

2. Component isomerism.- included under chemical isomerism but distinct from

3. Pseudocomponent isomerism.- which supposes a change of structure within the molecule, the idea conveyed by the term dynamic isomerism or tautomerism.

1. Limiting phase or physical isomerism further, Kruyt says the substances can exist together in contact only at one point. One form may pass into the other, say with change of temperature, but on reversal of the conditions to former state the first form is again produced. Such a case is that of ice and water. Pure ice and pure water can exist together only at the melting point of ice. In some cases as with different dydrates of a salt, which are not true isomers but illustrate the point, one may be labile toward the other form; but the one form can always be obtained from the other by seeding. The change here is molecular.

2. As a rule no difficulties are presented with chemical isomerism because the isomers may exist together under a wide variety of conditions unless they react with

one another. Such isomerism is exhibited in the case of the alcohols and ethers, for instance, dimethyl alcohol and ethyl alcohol; that is, their formulas coincide but the compounds belong to different classes. In most cases such isomers can be recognized or separated by class reactions. In no case is one readily obtainable from the other without the action of some reagent.

3. Dynamic isomerism is more complicated; in that the change is due to a shifting of an atom or a group of atoms within the molecule; hence, chemical methods avail but little. The two forms are readily often spontaneously interconvertible. The behavior of such ''pseudocomponents'' will vary;, dependent upon whether or not equilibrium is reached. But if equilibrium is established all phenomena cease though one compnnent may react with one reagent and the other with another. The classical illustration of this is acetoacetic ester which is a distinct type of isomerism.

Acetoacetic ester reacted in many ways as an alcohol,for instance with metallic sodium, but in many more ways it reacted as a ketone, yielding a secondary

alcohol on reduction. It was finally determined that the liquid ester was an equilibrium mixture of the two with the enol or hydroxy form the more labile. This most important kind of isomerism is known as the keto-enol type.

A strongly ionizing solvent, for instance, alcohol or water, will favor the formation of the keto form, while benzene determines the enol form. It has been suggested the enol compound, in the case of alcohol as a solvent, was formed, but the alcohol having an ionizing action on the dissolved substance dissociated it, forming hydrogen ions and an organic ion. The organic ion would then recombine with the hydrogen ion in the nonionizing keto form. While with benzene as a solvent, the enol form remains constant since no ionizing action is exerted on the phenol.

Biilmann[1] has criticized this classification of Kruyt's but has set no better criteria himself. He claims that there are in general but two kinds of isomerism. If isomeric substances having identical structure and

[1] B. 7, 827(1911)

composition they are polymorphs. . If they are structurally different, the case is one of tautomerism. Furthermore, if no observations show isomerism, the case must be called polymorphism.

Stobbe[1] has described a kind of dynamic isomerism which he calls thermochromism which is of interest in connection with the yellow and white salts. He found that with some compounds there was a gradual change of color with a rise in temperature and the action was reversible. That is,the substance went through the same changes on cooling. Hantzsch explained this as the solution of various amounts of the two isomers in one another as equilibrium is disturbed. Mercuric iodide exhibits a change from red to yellow but this change is not gradual, therefore, the two forms are not dynamic isomers but polymorphs. On the other hand, each in turn loses color by treatment with liquid air so here both the red and the yellow show thermochromism.

Cohen in his ''Organic Chemistry'' has devoted a chapter to a summary of views on tautomerism. He

.....

1 Ann. 380, 17 (1911)

regards ''dynamic isomers'' as meaning reversible isomeric change that is, they are more readily interconvertible than other isomers, in fact, equilibrium may exist without the action of any agent.

As to the mechanism of isomeric change, Larr believed it to be intra-molecular; Lowry maintains that a third substance acting as a catalyst is necessary. Baly and Desch in studying absorption spectra found that whereas an hydroxyl radical or the presence of a double bound was not indicated by banded spectra yet they found banded spectra in the ultra violet portion with acetoacetic ester, its metallic compound and other dynamic isomers; none however, with pure enolic or ketonic forms. Therefore, they conclude there is vibration within the molecule, but it cannot be due to a hydrogen atom or a metal because the oscillation frequency was in all cases the same. Hydrogen and the heavier metals would hardly vibrate in the same frequency.

Again some believe isomeric change to be due to the catalytic action of hydrogen ions. But as Cohen says

there is no evidence to prove this nor sufficient evidence to prove that the change is an intermolecular rather than an intramolecular one.

It now remains to be seen where the compound studied is to be placed. First of all it is not a case of physical isomerism for the simple reason that the two forms must exist at only one temperature; but as has been shown both forms appeared in the dry acetone solution in the experiments with solid potassium hydroxide. Both forms existed under reduced pressure and in the presence of moisture.

Secondly, they are not chemical isomers as ethyl alcohol and methyl ether though they both exist under widely varying conditions, they are mutually convertible without reagents. Chemical isomers are not thus interconvertible.

It might possibly be a case of dynamic isomerism which seems to fit all the requirements of the case that we know. It now remains to place it within the limits of a particular type.

Thermochromism might be the solution of the matter since the change from white to yellow is gradual and the same phenomena recur on cooling. Buth both exist atmone temperature in acetone. Moreover, such a type is a mere labelling anf throws no light on the molecular action within the compound.

It could be a case of polymerism which Kruyt considers as a kind dynamic isomerism. The only argument possible as yet against this, is that the white should probably be the simple ordinary form and the yellow the polymeric form. Now according to Ostwald's generalization the unstable form should appear first. Polymers are more stable than the monomolecular form almost invariably, hence the monomolecular form appears first. But in the precipitation by potassium ethylate in benzene, the yellow form appears first and not the white form. Of course molecular weight determinations would settle this question, but water is the only solvent which seems to dissolve both forms to any extent and phenol salts are too largely hydrolyzed in water for this solvent to be

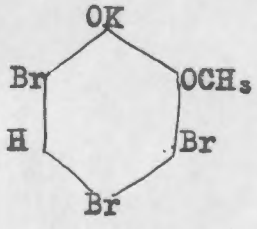
useful.

The more convincing category under which to place the salts is the keto-enol type. Phenols without a nitro group may exist in the keto form, though the enol one is usually the more stable. This, then, would seem to explain the case at hand. It eas before stated that a strongly ionizing solvent, alcohol or water, tended to produce the keto form, while benzene which ionized but slightly produced the enol form. It will be remembered that in all cases where a permanent yellow compound was obtained, alcohol was present. Might not then the yellow salt be the keto form? So far experimentally, it has been the less stable form appearing first always. On the other hand, alcohol, water or acetone produced either solid white salt or a solution of it. This, then, would represent the enol or the more stable usual form of a phenol salt.

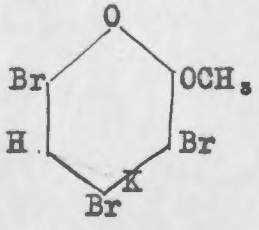
If this keto-enol isomerism is not the true explanation it would rather seem as though there must be a new isomerism here. Rather than try to explain how this could be it seems better to consider the case as

one of keto-enol isomerism until further work has been done on the subject.

In the meantime considering this the case, we may look into the possible structure of the salts. In the white or enol form the potassium atom would be tied to oxygen. In the yellow salt it would be tied to carbon as in the following graphic formulae:



White



Yellow

Experimental Part.

Preparation of the Phenol.- At first ten grams of guaiacol were dissolved in chloroform and the calculated amount of bromine was added from a burette, allowing five tenths of a cubic centimeter access. The whole was let stand for two hours, precipitated with water and filtered. The phenol was then dissolved in alcohol, water was added to a slight precipitate and the whole heated to boiling. From this solution tribromguaiacol crystallized out on cooling, These first crystals were rarely pure while the yield from the mother liquor was small and unsatisfactory. Further crystallization increased the purity of the product but the yield was very low, while the phenol showed a tendency to come down in an amorphous condition.

Consequently the guaiacol was next dissolved in glacial acetic acid, a sufficient bulk being used to hold in solution. The new phenol form bromine was then added from a burette. The product was then allowed to stand, precipitated with water and filtered. For some time the product was crystallized from ninety five per cent

alcohol. Later it was dissolved in alkali and precipitated by glacial acetic acid; this method being found equivalent to several crystallizations from alcohol.

Much later in the work it was found that the color, imparted to solvents by slightly impure phenol, could be removed by Fuller's earth.

Some time was spent in obtaining tribromguaiacol pure enough to give a colorless acetone solution in sufficient quantity to work with. It seemed then as though the chemically pure phenol was faintly pinkish rather than dead white, though no further effort was made to settle this definitely.

As by far the greater amount of time was spent on the preparation and analysis of the potassium salt of tribromguaiacol only a brief account of the other alkali preparations will be given.

Ammonium Salt.- This salt was never made except by the direct action of dried ammonia on a solution of the phenol in benzene. Almost immediately a white crystalline product resulted. After the reaction was completed the salt was removed, washed with alcohol to remove any phenol, then with ether, and dried in a dessicator. One sample was air-dried, no physical change was noted.

A weighed sample of the salt was dissolved in water and titrated with tenth normal hydrochloric acid, using methyl orange as an indicator.

.6369 grms. required 7.86 cc. $\frac{n}{10}$ HCl

Found NH_3 - 4.16 o/o

Calc.(anhydrous) 4.51 o/o

Two samples analyzed for bromine

.1311 grms. gave .1962 grms. AgBr

Found 63.69 o/o

Calc. 63.49 o/o

.2000 grms. gave .3013 grms. AgBr

Found 64.11 o/o

Two weeks later

.1560 grms. gave .2376 grms. AgBr . Found 65.31 o/o

showing that ammonia was probably lost on standing in the dessicator. This is not at all surprising in the ammonia salt of a phenol.

The salt showed no change in color on heating but very likely lost ammonia since it melted sharply at 118° a point but little above the melting point of tribromguiacol.

Sodium Salt.- The sodium salt was prepared at first by adding dried sodium hydroxide to a solution of the phenol in acetone. The resulting compound was white but free sodium hydroxide was present, so nothing was done more than note the color of the salt.

Later, clean metallic sodium was added in small quantities to absolute alcohol, the flask being cooled from time to time. A quantity of tribromguaiacol was dissolved in benzene and the sodium ethylate added directly. A copious precipitate of the sodium salt separated out immediately. It was removed from the flask, washed with benzene and then with absolute alcohol.and dried in a vacuum dessicator. This salt was found to be very stable.

Samples titrated for sodium, with methyl orange as an indicator resulted as follows:-

.1999 grms. required 2.73 cc. $\frac{n}{10}$ HCl

Found Na 6.35 o/o

Calc. (anhydrous) 5.95 o/o

.4365 grms. required 5.28 cc. $\frac{n}{10}$ HCl

Found 5.61 o/o

.3105 grms. required 3.64 HCl

Found 5.73 o/o

Bromine

.1322 grms. gave .1882 grms. AgBr

Found Br = 60.77 o/o

Calc. 62.65 o/o

.2070 grms. .2997 AgBr

Found 61.61 o/o

In the solid form this salt turned yellow on heating to a temperature a little below the point of decomposition, but on solution it remained colorless.

Potassium Salt.- As before mentioned, most of the time was spent in studying the colored potassium salt, both with the idea of getting pure yellow salt, and studying the effect of change in solvent, concentration and temperature.

Experiments in Acetone.- A small amount of tribrom-guaiacol in a test tube was dissolved in freshly distilled acetone and solid potassium hydroxide crystallized from alcohol was added. A yellow precipitate mixed with white was formed; the salt adhering to the potash being yellow but it turned white on removal from acetone. With the slightest trace of impurity in the phenol the entire product was discolored.

Dried potassium hydroxide(over phosphorous pentachloride) or washed with acetone was used and in all cases a mixture of salts resulted. Then dried acetone was used, and finally freshly distilled dried acetone from the bisulphide compound, with no better results.

The mixture of the two salts was then taken and a solvent for one sought.

With water-- white)
Alcohol -- white) less soluble

Water and acetone--soluble but yellow) changed slowly to white
Acetone and alcohol-soluble but yellow)

Experiments in Water.- Acetone as a solvent for the phenol was then abandoned, and potassium hydroxide was put in a water solution, the phenol being added directly to the solution. There was no action unless it was heated when the yellow salt was formed but was insoluble in alkali at this concentration. Then a series of experiments with various dilutions was made as follows (pure tribromguaiacol being used in 1/2 grm. quantities)

	Strength of KOH	Character of ppt.
5 cc.	30 o/o	Yellow, white on cooling.
''	20 o/o	'' ''
''	15 o/o	'' ''
''	10 o/o	'' ''
''	7.5 o/o	'' but goes into sol.
''	5 o/o	'' ''

A water solution of the salt was heated, to see at what temperature the first yellow appeared the original solution being almost colorless. At 45° the first yellow was noticed while at 58° the solution was distinctly yellow. The same phenomena occurred on cooling. Various concentrations were used but did not affect the temperature point of color appearance& All salts were white on cooling.

Experiments in Alcoholic Potash.- Alcohol as a solvent for potassium hydroxide was then used. A small quantity was added to a twenty five per cent solution of the potash in absolute alcohol. Whitish-yellow salt resulted.

The phenol was then dissolved in absolute alcohol free from aldehyde and the potassium hydroxide dissolved in alcohol of thensame purity. A yellowish-white salt was formed but was of considerable quantity so it was washed with alcohol and acetone and dried in a vacuum dessicator. Portions of the salt were treated with the following alkaline reagents:-

Reagent	Char. of product.
KOH	Unchanged
NaOH	"
Na_2CO_3	"
$(NH_4)_2CO_3$	Whitish
Na_2HPO_4	White
$NaHCO_3$	Unchanged
H_2O	"

A ten per cent solution of alc. pot. was added to an alcoholic solution of the phenol and a yellow crystalline product resulted but this turned white on washing. This sample had but a small amount of yellow present while the product before mentioned was predominantly yellow. A weighed quantity of each was placed in small platinum boats and inserted in a glass tube. Dried carbon dioxide was passed through for some time. No change of weight or color occurred in the compound.

Experiments in Methyl Alcohol.- Solid potassium hydroxide was then added to a solution of the phenol in methyl alcohol; the salt was bright yellow but contained

free potassium hydroxide. So alcoholic potash was used. A product containing but little white salt was obtained, the sample remained apparently unchanged for a month in air.

Ether.- The phenol was dissolved in ether dried over sodium and solid potassium hydroxide added. Worked to give yellow salt which turned white on exposure to air.

Experiments in Benzene.- Solid potassium hydroxide in pure benzene gave a bright yellow crystalline compound. Here the purity of the phenol had much to do with the character of the product, the slightest trace of impurity yielding a dark color in the benzene solution. The solid potassium hydroxide was always unsatisfactory so alcoholic potash was added to the benzene solution. A yellow precipitate resulted, it was removed and let stand with a fresh solution of the phenol in benzene to remove any access of potassium hydroxide. It was then washed with benzene and finally with absolute alcohol and dried in a dessicator. This salt remained comparatively yellow even on exposure of air. Accordingly, it was analyzed for

potassium.

One sample titrated directly,

.3100 grms. required 3.45 cc.---- $\frac{n}{10}$ HCl

Found 8.78 o/o

Calc. (anhydrous) 9.81 o/o

Two samples treated with sulphuric acid for potassium

2.0176 grms. gave .473 grms. potassium sulphate.

Found 10.53 o/o

.5283 grms. gave .1314 grms. potassium sulphate

Found 11.17 o/o

Results of analyses showed an access of potassium present.

This product from benzene and alcoholic potash was treated with methyl iodide on a reflux condenser for one hour. An orange yellow solid resulted. This was treated with alcohol in which it was easily soluble. The solution was evaporated and the crystals extracted with benzene, a yellow residue remaining. The benzene solution yielded fine white needles of the normal ether.

Experiments with Potassium Ethylate.- After some time when the sodium salt had been made directly from the metal, metallic potassium was used to prepare the yellow salt.

Clean metallic potassium was added in small pieces to absolute alcohol and the solution constantly cooled. The slightly impure phenol then at hand colored the benzene too much for use, so Fuller's earth was tried and found to remove all traces of color. To such a solution of phenol in benzene a few drops of potassium ethylate were added. After a short time bright yellow crystals formed. These were filtered off, since it was feared that an access of phenol was necessary for this yellow compound. An access of the potassium ethylate solution was then added to the remaining phenol and a large amount of bright yellow salt wasobtained. The samples were analyzed separately but there was no apparent difference in their composition. Both were washed with benzene and dried in a vacuum dessicator, both remained yellow. Another sample which gave closer results was washed several times with benzene and then with absolute alcohol.

Results of analyses.

.1455 grm. gave .2041 AgBr

Found 60.11 o/o

Calc.(anhydrous) 59.69 o/o

Potassium

.3752 grm. gave .0780 grm. potassium sulphate

Found 9.33 o/o

Calc. 9.81 o/o

.7853 grm. gave .1798 grm. potassium sulphate

Found 10.28 o/o

All the yellow salts obtained could be heated without apparent change to 230° when charing and gradual decomposition took place.

Potassium Salt of Dibromguaiacol.- It was obtained from solid potassium hydroxide and the phenol in an acetone solution. The salt formed was white and did not change with heat.

Potassium Salt of Tribromresorcin Monomethylether.- It was obtained from alcoholic potash and the phenol in benzene. The precipitate was dark colored and readily decomposed.

Potassium Salt of Tetrabromguaiacol.- It was obtained from solid potassium hydroxide and the phenol in benzene. Precipitate white but immediately grew dark. Later it was made from potassium ethylate and the phenol in benzene. Yellow crystalline precipitate soluble in water.